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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte COHAVA GELBER and KATHLEEN ROUSSEAU

Appellants

Appeal 2009-1107
Application 10/632,878
Technology Center 1600

Decided[1]: April 29, 2009

Before RICHARD TORCZON, SALLY GARDNER LANE, and MICHAEL P. TIERNEY *Administrative Patent Judges*.

LANE, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

I. STATEMENT OF THE CASE

The appeal, under 35 U.S.C. § 134, is from a Final Rejection of claims 1, 3-36, and 38. Claims 2 and 37 have been cancelled. (App. Br. 2). We affirm.

Appellants claim methods of enhancing transport of a compound across a cell membrane by forming a complex with diketopiperazine ("DKP") and contacting the cell.

The Examiner relied on the following patent documents.

Name	Number	Date
Steiner '497	6,071,497	June 6, 2000
Steiner '885	6,652,885	November 25, 2003

The Examiner rejected claims 1, 3-6, 8-18, 20-24, 26, 28, 33-36, and 38 under 35 U.S.C. § 102(b) over Steiner '497. The Examiner rejected claims 1, 4-10, and 13-36 under 35 U.S.C. § 102(e) over Steiner '885. The Examiner also rejected claims 1, 3-36, and 38 under 35 U.S.C. § 103(a) over Steiner '497 and Steiner '885. We review claim 1 as a representative claim. *See* Bd. R. 37(c)(1)(vii).

Appellants argued separately for the patentability of claims 4, 11, 12, 33, and 38, as a group, and of claim 13. We review claims 38 and 13 as representative claims.

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II. LEGAL ANALYSIS

"During examination, 'claims ... are to be given their broadest reasonable interpretation consistent with the specification, and ... claim language should be read in light of the specification as it would be

interpreted by one of ordinary skill in the art.'" *In re American Academy of Sci. Tech Center*, 367 F.3d 1359, 1364 (Fed. Cir. 2004).

"Anticipation requires a showing that each limitation of a claim is found in a single reference, either expressly or inherently." *Atofina v. Great Lakes Chem. Corp.,* 441 F.3d 991, 999 (Fed. Cir. 2006).

"[I]t is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." *In re Swinehart*, 439 F.2d 210, 212-13 (CCPA 1971); *see also In re Cruciferous Sprout Lit.*, 301 F.3d 1343, 1352 (Fed. Cir. 2002) ("the prior art inherently contains the claim limitations that Brassica relies upon to distinguish its claims from the prior art. While Brassica may have recognized something about sprouts that was not known before, Brassica's claims do not describe a new method.) "[A]fter the PTO establishes a prima facie case of anticipation based on inherency, the burden shifts to appellant to 'prove that the subject matter shown to be in the prior art does not possess the characteristic relied upon. [citing *Swinehart*].'" *In re King*, 801 F.2d 1324, 1327 (Fed. Cir. 1986).

III. ISSUES

1. Does the prior art teach the steps of "forming a complex comprising [a] compound and an effective amount of diketopiperazine (DKP)" and "contacting [a] cell *in vivo* with the complex?"

2. Have Appellants provided sufficient evidence to show that when these steps are performed they do not inherently "enhanc[e] transport of a compound across a cell membrane comprising a lipid bilayer?"

IV. FINDINGS OF FACT

1. Appellants' claim 1 recites[2]:

> A method for enhancing transport of a compound across a cell membrane comprising a lipid bilayer, comprising
>
> forming a complex comprising the compound and an effective amount of diketopiperazine (DKP) to enhance transport of the compound directly into the cell, wherein transport of the compound is increased in the presence of the DKP compared to in the absence of the DKP, and
>
> contacting the cell *in vivo* with the complex.

(App. Br. 21, Claims App'x).

2. Appellants' specification teaches that "the compound can be a peptide such as insulin or . . . [c]alcitonin . . . ." (Spec. 4, ll. 26-27).

3. Appellants' specification teaches that "[a] method of delivering a composition to a specific site in a human or other mammal is carried out by contacting cells or a tissue with a complex containing the compound and DKP. . . . In one embodiment, the compositions are administered by inhalation." (Spec. 10, ll. 14-21).

4. Steiner '497 teaches "[a]dministration of calcitonin-diketopiperazine micoparticles to sheep[,]" wherein "[a] suspense [sic] of diketopiperazine microparticle/sCT[3] . . . was instilled in each lung of each sheep." (Steiner '497 col. 11, ll. 10-11; 16-18).

5. Steiner '885 provides Example 2, entitled "Bioavailability of Insulin in Diketopiperazine Pulmonary Formulation," which teaches "inhalation of 100 U of TECHNOSPHERE™/Insulin" by humans and notes

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[2] Claim 1 has been reformatted to indicate the steps of the method. (*See* 37 C.F.R. § 1.75(i)).

[3] We understand "sCT" to mean salmon calcitonin. (*See* App. Br. 8).

that TECHNOSPHERES™ are "microparticles (also referred to herein as microspheres) formed of diketopiperazine that of [sic] self-assembles into an ordered lattice array at particular pHs . . . ." (Steiner '885 col. 11, l. 58, through col. 12, l. 65).

6. Steiner '885 teaches that

> insulin is administered via pulmonary delivery of microparticles comprising fumaryl [DKP] and insulin in its biologically active form. The charge on the insulin molecule is masked by hydrogen bonding it to the [DKP], thereby enabling the insulin to pass through the target membrane. This method of delivering insulin results in a rapid increase in blood insulin concentration that is comparable to the increase resulting from intravenous delivery.

(Steiner '885 col. 3, ll. 50-58).

V. ANALYSIS

35 U.S.C. § 102

Claim 1

Appellants' claim 1 recites a method comprising "forming a complex comprising [a] compound and an effective amount of diketopiperazine (DKP)" and "contacting [a] cell *in vivo* with the complex." (FF 1).

Steiner '497 teaches forming a complex comprising calcitonin, which is acknowledged in Appellants' specification to be a "compound" (FF 2), and DKP and administering this complex to a sheep's lungs. (FF 4). Thus, even though Steiner '497 does not teach that DKP enhances transport of a compound across a lipid bilayer cell membrane, it teaches the method steps recited in Appellants' claim 1.

Steiner '885 teaches these steps with an insulin/DKP complex in humans (FF 5) and explains that the DKP enables the insulin to pass through the target membrane, resulting in increased blood insulin concentration. (FF 6). Thus, Steiner '885 expressly teaches the limitations of the Appellants' claim 1.

Appellants argue that even though Steiner '497 and Steiner '885 report that the DKP microparticles were effective at causing absorption of the compound into the blood, "[a] discussion of blood plasma levels does not disclose or suggest administration of a compound through a cell membrane and directly into the cell." (App. Br. 8 and 12). According to Appellants, Patton, et al., "*The Lungs as a Portal of Entry for Systemic Drug Delivery*," Proc. Am. Thor. Soc., vol. 1, pp. 338-44 (2004) ("Patton") demonstrates that "generally, 'exogenous macromolecules are thought to be absorbed from the airspaces nonspecifically'" and that "the 'precise mechanisms of macromolecule absorption in the lungs are not well known.'" (App. Br. 9 and 12). Appellants also argue, among other reasons, that Steiner '497 teaches the specific mechanisms of phagocytic uptake and antibody binding of DKP-complexes, but that neither of these is "equivalent to transport of a compound across a cell membrane." (App. Br. 9).

We do not find Appellants' argument persuasive against Steiner '885 because it teaches transport across a cell membrane. (FF 6). Furthermore, Steiner '497 teaches the same steps as those recited in Appellants' claim 1 and so inherently anticipates claim 1. *See Swinehart,* 439 F.2d at 212-13. Therefore, it is Appellants' burden to show that these steps would not inherently "enhanc[e] transport of a compound across a cell membrane comprising a lipid bilayer" (FF 1), as claimed. *See In re King*, 801 F.2d at

1327. Appellants have not met this burden. Appellants have not cited portions of Patton or other evidence that addresses the effects of DKP in the sheep lung and show that it does not enhance transport across a lipid bilayer membrane. Merely citing possible ways that compounds can be absorbed in the lungs does not meet Appellants' burden to show that the enhanced transport would not inherently occur upon performing the claimed steps. Accordingly, Appellants' arguments are not persuasive.

Claims 4, 11-13, 33, and 38

Appellants argued separately for the patentability of claims 4, 11, 12, 33, and 38, as a group, and for the patentability of claim 13. (App. Br. 9-10).

7. Appellants' claim 38 recites: "The method of claim 1, wherein the cell is contacted with the complex in a schedule resulting in substantially no increase in the cell's immune response." (App. Br. 24, Claims App'x).

8. Appellants' claim 13 recites: "The method of claim 1, wherein DKP does not engage a toll-like receptor." (App. Br. 22, Claims App'x).

9. Appellants' specification provides that

> [t]he dose of insulin given in one treatment far exceeds the amount of peptide used to elicit an immune response. Rather then inducing an immune response, the administered dose induces immune nonresponsiveness (e.g., tolerance, clonal anergy). For example, peptide administered in the microgram dose range (e.g., 50 microg) (example i.m. vaccine) stimulates an immune response, whereas 5 mgs or 10 mgs of Insulin/FKDP complexes given by inhalation is expected to not result in stimulation of an immune response.

(Spec. 18, ll. 19-25).

10. Appellants' specification provides examples showing that DKP and DKP complexed with insulin are not immunogenic, even when administered in several different schedules, such as daily or once a week. (See Spec. 11, l. 21; 12, ll. 2-3; 13, l. 30, through 14, l. 2; 14, ll. 13-15; 18, ll. 10-11; 18, ll. 19-25).

11. Appellants' specification teaches that DKP does not engage toll-like receptors. (Spec. 13, l. 30, through 14, l. 2).

The contested dependent claims use wherein-clauses, which are analytically similar to whereby-clauses in that they specify an intended result of a method or functional limitation. "A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." *Minton v. Nat'l Ass'n of Securities Dealers, Inc.* 336 F.3d 1373, 1381 (Fed. Cir. 2003). We understand, though, that "when the 'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." *Hoffer v. Microsoft, Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005).

Appellants' claim 38 contains language requiring that the method of claim 1 includes contacting that does not increase the cell's immune response. (FF 7). Appellants' claim 13 contains language requiring that the cell of claim 1 does not engage a toll-like receptor. (FF 8). We understand that the effects of no increase in immune response and no engagement of a toll-like receptor to be intended results of contacting the cell with the complex. Indeed Appellants' specification, discloses that DKP and DKP complexed with insulin are not immunogenic (FF 9), even under several

different schedules of administration (FF 10), and that DKP does not engage toll-like receptors (FF 11). Thus, this language of claims 38 and 13 merely expresses an intended result and does not limit the scope of claim 1.

Appellants argue that "the '497 patent contains no disclosure relating to preventing an increase ina cell's immune response, much less how to achieve this" (App. Br. 10) and that "[t]here is nothing in []the ['']885 patent about avoiding an immune response, much less how to achieve this" (App. Br. 13). Similarly, Appellants argue that neither the '497 nor the '885 patent discusses engagement of DKP with a toll-like receptor. However, contacting the cell with the claimed complex as disclosed in the prior art would result in the effects of no increase in immune response and no engagement of a toll-like receptor. Appellants have not directed us to evidence to the contrary, e.g., evidence showing that the teaching in Steiner '497 and Steiner '885 of administration of a DKP/complex to sheep or humans lungs would be expected to cause an increase in the immune response or to engage toll-like receptors.

Appellants argue that Steiner '497 "teaches away" from a lack of immune response because "it discloses methods for increasing a cell's response by delivering an antigen." (App. Br. 11; emphasis in original). Appellants did not cite to a specific portion of Steiner '497 as support for their assertion. To the extent that Steiner '497 teaches specific genes that can stimulate an immune response (*see* Steiner '497, col. 9, ll. 36-40), we do not read this as discouraging one from expecting that DKP itself does not cause in increase in immune response or engagement with a toll-like receptor. *See In re Gurley*, 27 F3d 551, 31 USPQ2d 1130, (Fed. Cir. 1994) ("A reference may be said to teach away when a person of ordinary skill,

upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.").

Thus, the wherein clauses of claims 38 and 13 do not distinguish the claimed method over the prior art and we are not persuaded that claims 38 and 13 are separately patentable over claim 1.

35 U.S.C. § 103(a)

12. Steiner '885 states that

> U.S. Patent No. 6,017,497 to Steiner, et al. discloses microparticle drug delivery systems in which the drug is encapsulated in diketopiperazine microparticles . . . . The patent does not describe monomeric insulin compositions that are suitable for pulmonary administration, provide rapid absorption, and which can be produce in ready-to-use formulations that have a commercially useful shelf-life.

(Steiner '885 col. 2, ll. 58-67).

The Examiner rejected claims 1, 3-36, and 38, all of the pending claims, under 35 U.S.C. § 103(a) over the Steiner '497 and Steiner '885. Noting that both references teach administering complexes of a compound and DKP by inhalation, the Examiner found that there was motivation to combine them because Steiner '497 is referenced in Steiner '885 as a starting point for applications of the delivery system taught in Steiner '497. (*See* Ans. 5; *see also* FF 13). Furthermore, the Examiner concluded that

> [i]t would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum ratios, doses, rates of administration, etc. for the claimed composition

> of the instant application, because the component ratios, doses, rates of administration, etc. are an art-recognized result-effective variable that is routinely determined and optimized in the composition/pharmaceutical arts. One would have an expectation for success based on the examples provided.

(Ans. 5-6). Thus, the Examiner has provided a reason to combine Steiner '497 and Steiner '885 (*cf.* App. Br. 19) and a basis for a reasonable expectation of success in the combination. "[W]hen a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int'l v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 282 (1976)).

Appellants provide arguments against the obviousness rejection that are similar to those they provided against the rejections under 35 U.S.C. § 102. Briefly, they argue that neither Steiner '497 nor Steiner '885 teaches enhancing transport across a lipid bilayer cell membrane. (*See* App. Br. 15-16 and 17-18). We have discussed the merits of these arguments above, concluding that they are not persuasive.

Appellants also raised arguments against the separate patentability of claims 38 and 13 that are similar to those raised against the rejections of these claims under 35 U.S.C. § 102. (*See* App. Br. 16-17 and 18-19). Again, we have discussed the merits of these arguments above, concluding that they are not persuasive.

VI. CONCLUSION

1. The prior art teaches the steps "forming a complex comprising [a] compound and an effective amount of diketopiperazine (DKP)" and "contacting [a] cell *in vivo* with the complex."

2. Appellants have not provide sufficient evidence to show that when these steps are performed they will not inherently "enhance[] transport of a compound across a cell membrane comprising a lipid bilayer."

VII. ORDER

Upon consideration of the record and for the reasons given,

the rejection of claims 1, 3-6, 8-18, 20-24, 26, 28, 33-36, and 38 under 35 U.S.C. § 102(b) over Steiner '497 is AFFIRMED;

the rejection of claims 1, 4-10, and 13-36 under 35 U.S.C. § 102(e) over Steiner '885 is AFFIRMED;

the rejection of claims 1, 3-36, and 38 under 35 U.S.C. § 103(a) over Steiner '497 and Steiner '885 is AFFIRMED;

no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2008).

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AFFIRMED

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